

UNKNOWN TO ME ON ONE OCCASION, THE MEMBER OF THE PEDIATRIC STAFF WHO HAD REFERRED A WILMS' TUMOR TO ME, TOOK FOUR MEDICAL STUDENTS ON ROUNDS TO FEEL THE MASS WHILE I WAS OPERATING ON THE PRECEDING CASE. WHEN I OPENED THE ABDOMEN, THE WILMS' TUMOR WAS RUPTURED AND FRIABLE MALIGNANT TISSUE WAS FOUND THROUGH THE RETROPERITONEUM; THE HEMORRHAGE HAD EXTENDED WELL TO THE CONTRALATERAL SIDE AND HAD MADE ITS WAY UP INTO THE MESOCOLON OF THE ASCENDING AND TRANSVERSE BOWELS. THAT PATIENT DIED.

ONE OF THE MOST HORRENDOUS SURGICAL PROCEDURES IN REFERENCE TO A WILMS' TUMOR THAT WE EVER UNDERTOOK WAS A NEPHRECTOMY IN CONJUNCTION WITH THE REMOVAL, VIA THE RENAL VEIN, OF A TUMOR THROMBOUS THAT EXTENDED UP THE VENA CAVA, TURNED THE CORNER, AND ENDED IN THE RIGHT ATRIUM. POSTOPERATIVELY, IN ORDER TO DEMONSTRATE, FOR TEACHING PURPOSES, WHAT WE HAD DONE, AND WHILE THE CHILD WAS STILL ON THE OPERATING TABLE IN A SUPINE POSITION, WE PLACED THE TUMOR NEXT TO HIM AT HIS RIGHT FLANK AND THEN LAID THE THROMBUS ON HIS BODY TO MIMICK ITS INTERNAL POSITION.

**IT STARTED AT THE LEVEL OF HIS LIGATED RENAL VEIN AND LAY
ACROSS HIS RIBCAGE AND TURNED AROUND TO END IN A
BULBUS MASS JUST OVER HIS RIGHT ATRIUM.**

**WHEN, A YEAR OR SO LATER, I WAS PRESENTING A PAPER AT THE
BOSTON CITY HOSPITAL AS PART OF A SYMPOSIUM ON CANCER
IN CHILDHOOD, I SHOWED THIS CASE, INCLUDING A
MICROSCOPIC SECTION OF THE TIP OF THE THROMBUS FOUND IN
THE ATRIUM.**

THERE WAS NO DOUBT THE THROMBUS WAS WILMS' TUMOR AND THAT WAS THE ONLY POINT I WAS TRYING TO MAKE. IN THE AUDIENCE, HOWEVER, WAS JUDAH FOLKMAN, THEN SURGEON-IN-CHIEF OF THE CHILDREN'S HOSPITAL OF BOSTON, AND A SCIENTIST WITH A LIFE-LONG INTEREST IN THE ANGIOGENESIS FACTOR. AMONG OTHER CONCERNS, HIS THESIS WAS THAT TUMORS CAN'T GROW WITHOUT BLOOD SUPPLY. WHERE DO THE BLOOD VESSELS COME FROM, AND WHAT TRIGGERS THEIR DEVELOPMENT?

I PUSHED A BUTTON ON THE PODIUM TO MOVE THE SLIDE AND
DR. FOLKMAN CRIED OUT, "WAIT, WAIT!" I BACKED THE SLIDE UP.
THERE HE DEMONSTRATED SOMETHING I HAD NOT SEEN. ON THE
VERY TIP OF THE THROMBUS, IN THE MIDST OF THE TELLTAIL
HISTOLOGY OF WILMS' TUMOR, THERE WERE TINY BLOOD
VESSELS GROWING MORE THAN TWO FEET AWAY FROM THE
PRIMARY TUMOR THAT GAVE BIRTH TO THE THROMBUS.



IT WAS, OF COURSE, THE ADVENT OF CHEMOTHERAPY THAT CHANGED THE WHOLE CONCEPT OF THE MANAGEMENT OF CHILDHOOD CANCER,--AND IT AFFECTED WILMS' TUMOR FIRST.

IT IS INTERESTING THAT UP UNTIL THE ADVENT OF CHEMOTHERAPY, ALL OF THE MAJOR CHILDREN'S HOSPITALS IN THE COUNTRY HAD ABOUT THE SAME SURVIVAL RATE FOR WILMS' TUMOR USING JUST ABOUT THE SAME PROTOCOL THAT I HAVE DESCRIBED. SEVERAL OF US HAD ACHIEVED 47 POINT SOMETHING % SURVIVAL BEFORE CHEMOTHERAPY. I KNOW OF NO ONE WITH A RESPECTABLE SERIES WHO REACHED 48%.

**UNTIL CANCER CHEMOTHERAPY GAINED A FOOTHOLD, THE
MANAGEMENT OF CHILDHOOD CANCER WAS THE SURGEON'S
DOMAIN, WITH AN ASSIST FROM THE RADIOLOGIST.**

**COLLEAGUES IN INSTITUTIONS SIMILAR TO MY OWN WERE NOT
ONLY SURGEONS AND PEDIATRICIANS, BUT FAMILY COUNSELORS
AND CHAPLAINS AS WELL. WITH THE ADVENT OF
CHEMOTHERAPY, THE SPECIALTY OF PEDIATRIC ONCOLOGY
CAME INTO ITS OWN. THERE IS NO DOUBT THAT BECAUSE OF
AVAILABLE RESEARCH FUNDING, THE INTEREST IN A NEW
FRONTIER, AND THE INCREASING SUCCESS WITH CHEMOTHERAPY
FOR WILMS' TUMOR AND RHABDOMYOSARCOMA (AS WELL AS
GREAT SUCCESS IN THE MANAGEMENT OF LEUKEMIA),
ONCOLOGY BEGAN TO ATTRACT MORE AND MORE BRIGHT YOUNG
PEDIATRICIANS AND HEMATOLOGISTS.**

I HAVE CONSIDERABLE PRAISE FOR MEDICAL ONCOLOGISTS AND THEIR ACCOMPLISHMENTS. I THINK, IN MANY INSTITUTIONS ACROSS THE LAND, WHAT COULD HAVE BEEN A MAJOR THRUST BY MANY DISCIPLINES INVOLVED IN THE MANAGEMENT OF THE JUVENILE CANCER PATIENT FELL SHORT OF THE MARK. AS THE ONCOLOGIST HAS RISEN, SO HAS THE PERCEPTION OF THE VALUE OF THE SURGEON FALLEN. IT WOULD BE TRAGIC, IF, WITH THE HISTORY OF THE PAST FEW YEARS, THE SURGEON IS RELEGATED TO THE POSITION OF TECHNICIAN TO THE MEDICAL ONCOLOGIST.

**IT IS IRONIC THAT MOST GOOD MEDICAL ONCOLOGISTS WERE
ATTRACTED TO THEIR PRESENT SUB-SPECIALTY BY THE
REPUTATION AND CASE LOAD OF A PEDIATRIC SURGICAL
CANCER ENTHUSIAST.**

**AS FASCINATING AS ALL CHILDHOOD MALIGNANT TUMORS WERE,
IT WAS THE NEUROBLASTOMA AND ITS PECULIAR LIFE HISTORY
THAT RIVETED MY ATTENTION,--EVEN EARLY ON.**

WHEN I DID MY RETROSPECTIVE STUDY OF RECORDS OF
DISCHARGE DIAGNOSES WITH MALIGNANT TUMORS, I HAD BEEN
~~WAS~~ STRUCK THAT 25% OF THEM WERE NEUROBLASTOMA. I
ATTEMPTED TO TRACE THESE CHILDREN, FOUND THAT MOST OF
THEM HAD DIED, BUT THAT SOME RATHER REMARKABLE
YOUNGSTERS HAD SURVIVED.

ONE HAD BEEN IN THE HANDS OF A NEUROSURGEON WHO HAD
DONE A LAMINECTOMY AND REMOVED A PORTION OF A HIGHLY
UNDIFFERENTIATED NEUROBLASTOMA, CLOSING THE PATIENT UP
TO DIE.

IN RETROSPECT I THINK EVERYBODY MISSED THE ABDOMINAL TUMOR, OF WHICH THE INTRASPINAL EXTENSION WAS THE SMALL END OF A DUMBBELL. SOME YEARS LATER WHEN SOMEBODY FELT AN ABDOMINAL TUMOR IN THIS NOW PARAPLEGIC CHILD, IT WAS BIOPSIED AND PROVED TO BE A QUITE BENIGN GANGLIONEUROMA. THE OTHER LIVING PATIENTS IN THAT SMALL GROUP OF NEUROBLASTOMA SURVIVORS IMPRESSED ME THAT THE THERAPY SEEMED TO HAVE HAD LITTLE OR NOTHING TO DO WITH SURVIVAL.

**OF COURSE I CAN ONLY SPEAK ABOUT THOSE CHILDREN AND
KNEW NOTHING ABOUT THE QUALITY OR QUANTITY OF
TREATMENT ON THOSE WHO DIED.**

**EARLY IN MY TENURE AT CHILDREN'S HOSPITAL, I WAS CALLED
UPON TO TREAT AN ABDOMINAL MASS IN THE INFANT SON OF A
FORMER RESIDENT WHO HAD MARRIED ONE OF OUR NURSES.
DURING SURGERY, I RUPTURED THE PSEUDOCAPSULE OF A
PERIRENAL NEUROBLASTOMA.**

IN ADDITION TO THAT POOR PROGNOSTIC SIGN, THE CHILD ALSO HAD MULTIPLE BARELY VISIBLE METASTASES TO THE LIVER, CONFIRMED BY BIOPSY. THE SURGERY WAS CERTAINLY NOT THE METICULOUS SURGERY OF CANCER THAT I HAD BEEN TAUGHT. THERE WAS GROSS SPILL OF TUMOR THROUGHOUT THE PERITONEAL CAVITY. I TOLD THE FAMILY THE SITUATION WAS HOPELESS AND NO RADIATION THERAPY SHOULD BE GIVEN.

SIX WEEKS LATER THE CHILD RETURNED FOR A POSTOPERATIVE VISIT AND HAD MULTIPLE SUBCUTANEOUS NODULES WHICH I ASSUMED TO BE TUMOR. I DID NOT ASK FOR A BIOPSY.

THE YOUNGSTER WAS SENT HOME TO DIE. THAT PATIENT
EVENTUALLY GRADUATED FROM LAW SCHOOL AND WHEN LAST
SEEN BY ME, THE PYELOGRAM SHOWED NOTHING MORE THAN A
DISTORTED CALYX OF ONE KIDNEY ON THE SIDE OF THE
SURGERY. ✓

A THREE AND ONE-HALF YEAR OLD GIRL WAS SENT TO ME WITH THE DIAGNOSIS OF SPLENOMEGALY. IT WAS OBVIOUS THAT THE MASS IN QUESTION WAS NOT A SPLEEN, BUT A TUMOR, AND AFTER SUITABLE WORKUP, ABDOMINAL EXPLORATION REVEALED A MALIGNANT NEUROBLASTOMA ARISING FROM THE ABDOMINAL SYMPATHETIC CHAIN, FASTENED TIGHTLY TO THE SPINAL COLUMN AND DIFFUSE ENOUGH IN THE RETROPERITONEUM AS TO BE NONRESECTABLE.

THE TUMOR WAS SOFT AND SUCCULENT, AND AFTER OPENING THE POSTERIOR PERITONEUM, IN THE COURSE OF BIOPSY, THERE WAS GROSS SPILL OF THE TUMOR INTO THE PERITONEAL CAVITY.

I PRESENTED THE FATHER WITH A HOPELESS PROGNOSIS AFTER WHICH HE BEGAN TO READ BROADLY ABOUT NEUROBLASTOMA,--WHAT LITTLE THERE WAS WRITTEN ABOUT IT,--AND BECAME AN ALLY WITH ME AGAINST THE TUMOR.

THE TUMOR SLOWLY ENLARGED AND ITS LOWER TIP, WHICH HAD BEEN PALPABLE JUST BELOW THE COSTAL CAGE, DESCENDED UNTIL IT REACHED THE PELVIS, TURNED TOWARD THE RIGHT, AND EVENTUALLY POINTED UPWARD IN THE RIGHT LOWER QUADRANT. AFTER A PERIOD OF STABILIZATION THERE, THE TUMOR SLOWLY RECEDED IN THE DIRECTION FROM WHENCE IT HAD COME UNTIL IT WAS BARELY PALPABLE HIGH UP UNDER THE COSTAL CAGE ON THE LEFT. BY THAT TIME, IT WAS THE FATHER, NOT I, WHO WAS PUSHING FOR ANOTHER LOOK.

THIS WE DID AND FOUND AN EXTREMELY FIRM, SMALL
GANGLIONEUROMA ABOUT THE SIZE OF A TENNIS BALL, WHICH I
RESECTED, WITHOUT BEING ABLE TO DETACH EVERY CELL FROM
THE SPINAL COLUMN. THE CHILD SURVIVED, AND WAS LOST TO
FOLLOW-UP IN HER TEENS.

THE SURVIVAL OF THOSE YOUNGSTERS FOLLOWING GROSS
SPILL OF THE TUMOR INTRAPERITONEALLY LED ME TO BELIEVE
THAT PERHAPS THE VERY SPILL MIGHT HAVE HAD A BENEFICIAL
EFFECT. AFTER MORE EXPERIENCE, MY FIRST PRESENTATION ON
THE SUBJECT OF NEUROBLASTOMA WAS BEFORE THE SOCIETY
OF UNIVERSITY SURGEONS IN 1955.

I ENTITLED THE PAPER "NEUROBLASTOMA IN CHILDHOOD: THE EFFECT OF MAJOR SURGICAL INSULT ON SURVIVAL." I REPORTED A 38% SURVIVAL IN MY EXPERIENCE THUSFAR.

IN A DISCUSSION FOLLOWING MY PRESENTATION, CRITICS SUGGESTED THAT IF ONLY I HAD BEEN SMART ENOUGH TO USE RADIATION THERAPY IN ADDITION TO SURGERY, I COULD HAVE IMPROVED MY RESULTS.

THE NEXT EIGHT NEUROBLASTOMAS I TREATED WITH RADIATION.
ALL OF THEM DIED. I THEN RETURNED TO MY LONG-HELD BELIEF
THAT THE ADJUNCT OF RADIATION THERAPY FOR
NEUROBLASTOMA DID NOT REALLY INCREASE SURVIVAL.
THIS POSITION, WHICH WAS LATER CLARIFIED BY THE WORK OF
MANY OTHERS, EVENTUALLY LED TO OUR UNDERSTANDING OF
THE CURRENT STAGING OF NEUROBLASTOMA. SOME
YOUNGSTERS, FOR EVERY SCIENTIFIC REASON, ENTITLED TO A
POOR PROGNOSIS AND ~~W~~ ON THEIR WAY TO DEATH, WERE
PATIENTS WITH STAGE IV-S DISEASE.

ONE OF THE MOST DIFFICULT THINGS FOR ME
TO SWALLOW PROFESSIONALLY WAS DISBELIEF.
SIDNEY FABER, DAN DANCO, & AUDREY
EVANS DID NOT BELIEVE. AFTER AUDREY
EVANS CAME TO CHOP - SHE HAD MADE
OPPORTUNITY TO SEE MY PATIENTS.
SEVERAL YEARS LATER AT A TEXAS MLC
MODERATED BY SIDNEY FABER - DANCO
ACKNOWLEDGED I WAS ⁶⁹ RIGHT - THAT WAS
THE FIRST TIME I KNEW I WAS BELIEVED
IT WAS ESTABLISHED

**THEIR PROGNOSIS WAS NOT IMPROVED BY RADIATION AND
THEIR SURVIVAL WAS ALMOST UNIFORMLY GOOD.**

**WHEN I LEFT THE PRACTICE OF SURGERY IN 1981 TO GO TO
WASHINGTON, MY OWN SURVIVAL RATE WAS THE SAME 38% THAT
MY PATIENTS ENJOYED IN 1955, IN SPITE OF ADJUNCTIVE
RADIATION AND CHEMOTHERAPY. UNFORTUNATELY,
NEUROBLASTOMA HAS NEVER HAD THE REMARKABLE
SUCCESSFUL INCREASE IN SURVIVAL THAT WAS ACCOMPLISHED
FOR WILMS' TUMOR WITH CHEMOTHERAPY.**

**I GUESS THE FIRST OF MANY SURGICAL AND PUBLIC HEALTH
CRUSADES OF MY LIFE CENTERED AROUND AWAKENING
PEDIATRICIANS TO THE POSSIBILITY OF DIAGNOSING CANCER IN
CHILDREN. IT'S HARD TO BELIEVE, ~~EVEN~~ AT THIS LATE TIME,
HOW DIFFICULT IT WAS TO FIND RECEPTIVE AUDIENCES AMONG
PEDIATRICIANS. AS I TRIED TO AROUSE A FEELING OF GUILT FOR
MISSING DIAGNOSES, BUT AT THE SAME TIME PROVIDING A WAY
OUT FOR THE IMPOSSIBLE PROBLEMS, I USED TO SPEAK OF
FOUR CATEGORIES OF TUMOR:**

- 1. THE VISIBLE OR PALPABLE LESION WHICH NO ONE COULD BE EXCUSED FOR MISSING;**
- 2. THE TUMOR THAT, BY ITS SYMPTOMATOLOGY, SHOULD AROUSE SUSPICION OF CANCER IF ONE INCLUDED IT IN THE DIAGNOSTIC POSSIBILITIES;**
- 3. THOSE TUMORS WHOSE SYMPTOMS MIMICKED OTHER MORE FAVORABLE DIAGNOSES (SUCH AS THE DIAGNOSIS OF RHEUMATIC FEVER, INSTEAD OF NEUROBLASTOMA);**
- 4. THE TUMORS HERALDED BY SUCH VAGUE SYMPTOMATOLOGY THAT NO ONE COULD BE BLAMED FOR A DELAYED DIAGNOSIS.**

**AS I LOOK BACK OVER THE LAST HALF-CENTURY, IT'S HARD TO
BELIEVE HOW LITTLE WE ALL KNEW WHEN I GRADUATED FROM
MEDICAL SCHOOL AND WHAT TREMENDOUS ADVANCES THERE
HAVE BEEN IN MEDICINE DURING MY LIFETIME.**

THE OPPORTUNITIES FOR LABORATORY AND CLINICAL INVESTIGATIONS OF CHILDHOOD CANCER ARE STILL LEGION. I STILL FEEL THAT IF SOMEONE COULD UNDERSTAND, IN ITS TOTALITY, THE BEHAVIOR OF NEUROBLASTOMAS, A KEY WOULD TURN IN MANY LOCKS IN OUR UNDERSTANDING OF ONCOGENESIS, MATURATION, AND SPONTANEOUS REMISSION. OF COURSE, ADJUNCTS TO THERAPY WOULD SOON FOLLOW. I THINK THAT COMBINATIONS OF ADJUNCTIVE THERAPY ALONG WITH SURGERY WILL CONTINUE TO LOWER MORTALITY RATES BUT ONLY SLOWLY WHILE INCREASING THE LONGEVITY OF CHILDREN DESPITE THE ULTIMATE FATAL OUTCOME. THE REAL BREAKTHROUGH, I THINK, WILL COME WITH A BETTER UNDERSTANDING OF THE IMMUNOLOGY OF CANCER AS WELL AS THE ELUCIDATION OF THE COMBINED FACTORS OF GENETIC PROPENSITY AND ENVIRONMENTAL STIMULI.

**WHILE THE DAY-TO-DAY CARE OF THE YOUNGSTER WITH THE
MALIGNANT TUMOR IS ONE OF THE ULTIMATE CHALLENGES IN
PEDIATRIC MANAGEMENT, THE IMPROVED SURVIVAL OF PATIENTS
WITH PEDIATRIC MALIGNANT TUMORS HAS BEEN ONE OF THE
OUTSTANDING SUCCESSES IN THE FIELD OF ONCOLOGY. IT HAS
BEEN A GOOD TIME TO BE ALIVE.**

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